GW26-e2202

An Novel Variant in the HNF4G Gene is Associated With Hyperuricemia in Chinese Han population

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OBJECTIVES Hepatocyte nuclear factor 4 gamma (HNF4G) is a protein binding to a DNA element of the transthyretin promoter in pancreas, kidney and small intestine. In a recent GWAS study, some SNPs in *HNF4G*gene are found to be associated with uric acid concentrations. The aim of the present study was to assess the association between the human *HNF4G* gene and hyperuricemia in Chinese Han population.

METHODS A total of 414 hyperuricemia patients and 406 gender and age-matched normouricemic controls were enrolled. Four single-nucleotide polymorphisms (SNPs) were genotyped as genetic markers for the human*HNF4G* gene (rs2977939, rs1805098, rs2941484, rs4735692). Data were analyzed for three separate groups: the total subjects, men, and women.

RESULTS For rs2941484 (SNP3), the genotype distribution in hyperuricemic subjects and was significantly different from that in normouricemic controls in total subjects (P=0.043) and men (P=0.038). Meanwhile, in recessive model of rs2941484, the distribution frequency of TT genotype and CC+CT genotypes also showed the significant difference between the hyperuricemia patients and normouricemic controls (P=0.012 in total subjects and P=0.011 in men). In men, after adjustments for SBP, DBP, fasting glucose, total cholesterol, triglycerides, LDL-C and creatinine, the people with the TT genotype of rs2941484 were found to have significantly higher chance of suffering from hyperuricemia than the ones with CT and CC genotypes (OR=1.887, P = 0.007).

CONCLUSIONS The results of this study indicate that the TT genotype of rs2941484 in the human *HNF4G* gene might be a gender-specific genetic marker for hyperuricemia in Chinese Han men.

GW26-e2215

Effects of Atorvastatin on JNK/AP-1 Signaling Pathway and the Expression of Related Factors in high glucose concentration-induced Vascular Endothelial Cells

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OBJECTIVES To study the effects of a atorvastatin on JNK/AP-1 signaling pathway and the expression of related factors in high glucose concentration-induced vascular endothelial cells.

METHODS HUVECs cultured in vitro were divided into blank control group(HG, 5.5mmol/L), the high glucose group(HG, 33 mmol/L), the atorvastatin group (HG 33 mmol/L+atrovastatin 10μmol/L). They were cultured with relevant drugs for 48 h. The enzyme linked immunosorbent assay (ELISA) was adopted to determine the content of TNF-α, IL-6, ICAM-1 and VCAM-1, and pJNK, pcJUN and AP-1 protein expressions were determined by western blotting assay.

RESULTS Compared with blank control group, the content of TNF-α, IL-6, ICAM-1 and VCAM-1 increased significantly in HG group ($P<0.05$), while pJNK, pcJUN and AP-1 protein expressions increased ($P < 0.05$). Compared with HG group, the content of TNF-α, IL-6, ICAM-1 and VCAM-1 in atorvastatin group decreased ($P<0.05$), while pJNK, pcJUN and AP-1 protein expressions decreased ($P<0.05$).

CONCLUSIONS Atorvastatin can inhibit JNK/AP-1 signaling pathway and the expression of related factors in high glucose concentration-induced Vascular Endothelial Cells.

GW26-e2253

An Imaging-based Renal Denervation Strategy in Hypertensive Canines Using Integrated Ultrasound Catheter

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OBJECTIVES Current renal denervation (RDN) procedures are criticized for their lack of targeted energy delivery and their clinical outcome should be improved. We aimed to access an imaging-based ablation strategy for RDN in hypertensive canine models using an integrated ultrasound catheter.

METHODS An ultrasound imaging probe and acoustic ablation transducer were integrated in an 8 F catheter to provide renal-arterial nerve ultrasonography and guided catheter-based acoustic RDN procedures. Ultrasonographic evaluation of renal innervation was conducted in 27 hypertensive dogs. Three dogs were killed for histological study, 20 were subjected to RDN using imaging-based site selection and 4 underwent sham procedure. In the RDN group, 4 dogs were killed immediately post RDN, while the rest were killed after 28 days for pathologic examinations. The blood samples were collected for further effects and safety evaluation in all animals before imaging and sacrificed.

RESULTS All of animals survived the procedure. The renal nerves exhibited linear-like echoes, and the distribution densities varied significantly across both the arterial regions and individual animals. In the RDN group, 170 of the 256 ultrasonographically observed sites with higher nerve densities were selected for ablation. An average energy emission of 10.6 times was delivered to the bilateral renal artery. The BP significantly decreased compared to the baseline (-12.6/-9.1 mmHg, $p<0.05$) and to the sham group at 28 days post-ablation. The plasma noradrenaline was decreased slightly but statistical significantly. The denervation effects were confirmed by pathological findings without significant acoustic ablation-related complications.

CONCLUSIONS The ultrasound imaging-based RDN ablation can be safely and effectively achieved in this hypertensive canine model. Thus, the individualized strategy should be explored as a novel procedure for improving RDN in clinical practice.

GW26-e4513

Histone demethylase JMJD2A inhibition attenuates neointimal hyperplasia in the carotid arteries of balloon-injured diabetic rats via transcriptional silencing: Inflammatory gene expression in vascular smooth muscle cells

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OBJECTIVES Diabetic patients suffer from serious neointimal hyperplasia following coronary interventions. The epigenetic abnormalities are increasingly considered to be relevant to the pathogenesis of diabetic complications. But the epigenetic mechanisms linking diabetes and coronary restenosis have not been fully elucidated. In this study, we explored the protective effects and underlying mechanisms of demethylases JMJD2A inhibition in balloon-injury induced neointimal formation in diabetic rats.

METHODS The chemical inhibitor 2,4-pyridinedicarboxylic acid (2,4-PDCA) and small interfering RNA (siRNA) were utilized to inhibit JMJD2A. *In vivo*, diabetic rat model was induced using high-fat diet (60% fat) and low-dose streptozotocin (35mg/kg). Diabetic rats underwent common carotid artery balloon injury followed with local transfection of siRNA-JMJD2A or intraperitoneal injection of 2,4-PDCA (7.5 mg/kg/d). The neointimal formation was evaluated using hematein-eosin (HE) staining. Immumohistochemical staining with specific antibody to proliferating cell nuclear antigen (PCNA) and H3K9me3 were conducted to assess cellular proliferation and modification of H3K9me3 in vivo respectively. The inflammatory response was detected using real-time PCR and western blot. *In vitro*, vascular smooth muscle cells (VSMCs) were pre-treated with 2, 4-PDCA (1.0 mM) or transfected with siRNA-JMJD2A (20nM), followed by stimulated by high glucose (HG). The proliferation and migration were detected to evaluate the function of VSMCs in response to HG. Real-time PCR and western blot were conducted to detect the expression of inflammatory genes (MCP-1 and IL-6). Chromatin Immunoprecipitation (ChIP) assay was performed to detect modification of histone H3 lysine9 tri-methylation (H3K9me3) at promoters of MCP-1 and IL-6.

RESULTS Both in HG-stimulated VSMCs and balloon-injured arteries of diabetic rats, JMJD2A was increased whereas H3K9me3 was decreased. JMJD2A inhibition attenuated neointimal formation of injured arteries in diabetic rats, in parallel with suppressed cellular proliferation. Compared with injury group, the inflammatory response (MCP-1 and IL-6) was repressed after JMJD2A inhibition, both in mRNA and protein expression. Importantly, immumohistochemical staining with anti-H3K9me3 indicated that there was elevated H3K9me3 in neointimal VSMCs. Complementarily *in vitro*, JMJD2A inhibition suppressed proliferation and migration in HG-stimulated